U.S. PATENT APPLICATION

FOR

METHOD FOR DETECTING AND CLASSIFYING A STRUCTURE OF INTEREST IN MEDICAL IMAGES

BY

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CROSS-REFERENCE TO RELATED APPLICATIONS

This application is cross-referenced to and claims priority from U.S Provisional Application 60/415,280 filed 09/30/2002, which is hereby incorporated by reference.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

The present invention was supported in part by grant number RO1 CA72023 from the National Institutes of Health (NIH/NCI). The U.S. Government has certain rights in the invention.

FIELD OF THE INVENTION

The present invention relates generally to medical imaging. More particularly, the present invention relates to methods for detecting and classifying a structure of interest in medical images to differentiate for instance (pre-)cancerous tissue from normal tissue.

BACKGROUND

Computed tomographic colonography (CTC) was first suggested in the early 1980s as a potential method for mass screening of colorectal cancer, the second leading cause of cancer deaths in the US. CTC was first realized in the 1990s following the rapid progress in computed tomography (CT) and in digital computing. CTC is a minimally invasive method that involves the steps of CT imaging the whole abdomen and pelvis after cleansing and air insufflation of the colon. Since the first realization, several studies have been conducted assessing the performance of CTC, mostly based on a radiologist's visual examination of either two-dimensional (2-D) CT images or three-dimensional (3-D) virtual colonoscopic views, or both. Most efforts have been directed toward developing better

visualization and navigation techniques, such as rendering, colon wall flattening, flight path planning algorithms, and user interface design. Recently some research has focused on developing computer-aided detection (CAD) methods for the identification of colonic polyps in 3-D CT data to improve the accuracy and efficiency of CTC. In these identification approaches, the 3-D geometrical features of polyps are extracted and used for their detection and identification. Mir *et al.* reviewed a set of methods proposed for shape description in CT images, e.g., moments, medial axis transforms, splines, curvature, Fourier descriptors, AR (Auto-Regressive) modeling, and statistical approaches (See A. H. Mir *et al.*, "Description of shapes in CT images: The usefulness of time-series modeling techniques for identifying organs," *IEEE Eng. Med. Biol. Mag.*, vol. 18, pp. 79–84, Jan./Feb. 1999). Summers *et al.* concluded that detection by shape analysis is feasible, especially for clinically important large polyps (See e.g. R. M. Summers *et al.*, "Automated polyp detector for CT colonography: Feasibility study," *Radiology*, vol. 216, no. 1, pp. 284–290, 2000; R. M. Summers *et al.*, "Automated polyp detection at CT colonography: Feasibility assessment in a human population," *Radiology*, vol. 219, no. 1, pp. 51–59, 2001). Paik *et al.* proposed to use a method based on overlapping surface normals to detect spherical surface patches along the colon wall that are likely to be parts of polyps (See e.g. D. S. Paik *et al.*, "Computer-aided detection of polyps in CT colonography: Free response ROC evaluation of performance," *Radiology*, vol. 217(SS), p. 370, 2000; D. S. Paik et al., "Detection of polyps in CT colonography: A comparison of a computer aided detection algorithm to 3-D visualization methods," in *Proc. 85th Scientific Sessions Radiological Society of North America*, vol. 213(P). Chicago, IL, 1999, p. 428). Yoshida *et al.* reported that geometric features extracted from small volumes of interest are effective in

differentiating polyps from folds and feces (See H. Yoshida *et al.*, "Detection of colonic polyps in CT colonography based on geometric features," *Radiology*, vol. 217(SS), p. 582, 2000), as well as characterizing colon wall surface geometry (See H. Yoshida *et al.*, "Three-dimensional computer-aided diagnosis scheme for detection of colonic polyps," *IEEE Trans. Med. Imag.*, vol. 20, pp. 1261–1274, Dec. 2001). Göktürk *et al.* fitted local spheres to the colon wall and based their detection on the existence of clusters of sphere centers (See S. B. Göktürk *et al.*, "A graph method for the conservative detection of polyps in the colon," in *Proc. 2nd Int. Symp. Virtual Colonoscopy*, Boston, MA, 2000).

Most of these prior methods are rather sensitive (i.e. ability to detect positives), but need to be more specific (i.e. ability to detect negatives) for clinical applicability. The low specificity of some of the previously reported methods is generally due to the assumption that high curvature surface patches occur only on polyps. While it is true for instance that polyps have highly curved surfaces, so do some other structures, like haustral folds and retained stool. Radiologists reading these images use additional information to classify suspicious regions. For example, haustral folds are elongated structures, as opposed to polyps, which protrude locally from the colon wall. Stool may sometimes be identified by relatively inhomogeneous image intensity compared to polyps. However, if an automatic CAD method results in a low specificity manual examination of a (large) number of images corresponding to the CAD outputs is required to ensure proper detection. Such an examination is costly, time consuming and inefficient. Accordingly, there is a need to develop a method that would be capable of increasing specificity without sacrificing

sensitivity. Such a method could also be used to enhance and classify outputs of a high-sensitivity low-specificity CAD method to eliminate false positives only.

SUMMARY OF THE INVENTION

The present invention is a method capable of detecting and classifying a structure of interest with a high specificity without sacrificing the sensitivity of detection. The method could be used as a stand-alone method or as a post-processing method to enhance and classify outputs of a high-sensitivity low-specificity method to eliminate false positives. The method is based on representing changes in 2-D cross-sections of three-dimensional image data with a vector field, characterizing the topology of this vector field and using the characterized topology of the vector field for detection, identification or recognition tasks of a structure of interest. A structure of interest is a structure of interest to a radiologist such as polyps (e.g. colonic polyps), nodules (e.g. liver and lung nodules), lesions, or the like.

More specifically, the method defines one or more image planes in a subvolume of a three-dimensional medical image. For each image plane, the edge displacement fields are computed for a plurality of slices that are defined over the axis perpendicular to its corresponding image plane. In general, one could define at least one image plane or a multiple set of image planes with each scrolling axis perpendicular to its respective/corresponding plane. In one exemplary embodiment, the image planes could be at least two mutually orthogonal planes. A more specific example could be the three

anatomical planes in which the scrolling axis is defined as the axis perpendicular to its respective plane, i.e. axial, sagittal, coronal. The edge displacement fields for all slices in an image field are combined to create an edge displacement field for that image plane. This combined edge displacement field is used to determine parameters. These parameters are then used to classify the structure of interest and determine whether the structure of interest is e.g. a polyp or a non-polyp. The classification could be based on the parameters from a single image plane or a combination of image planes. For instance, the three anatomical planes could be used to determine the parameters. In case three parameters are computed per image plane, one will end up with a 3x3 feature vector. The parameters could be further processed by taking for instance the average over the image planes for each parameter or by applying other functions or processes to combine the parameters and classify the structure of interest.

BRIEF DESCRIPTION OF THE FIGURES

The objectives and advantages of the present invention will be understood by reading the following detailed description in conjunction with the drawings, in which:

FIG. 1 shows an example of generating an axial edge displacement field demonstrated using a sphere according to the present invention;

FIG. 2 shows an example of three sequential axial images (smoothed for visual purposes) around a pre-detected structure and the associated EDF $\bar{v}_{axial}(x,y)$; and

FIG. 3 shows an example of axial EDFs of four cases: (a) positive (polyp) with [α; β; d] = [-0.96; 0.29; 4.99]; (b) positive with [α; β; d] = [-0.99; 0.12; 5.15]; (c) negative

(non-polyp) [α; β; d] = [-0.77; 0.65; 1.28]; (d) negative with [α; β; d] = [-0.71; 0.70; 0.72].

DETAILED DESCRIPTION OF THE INVENTION

Although the following detailed description contains many specifics for the purposes of illustration, anyone of ordinary skill in the art will readily appreciate that many variations and alterations to the following exemplary details are within the scope of the invention. Accordingly, the following preferred embodiment of the invention is set forth without any loss of generality to, and without imposing limitations upon, the claimed invention.

The method of the present invention could be referred to as an "Edge Displacement Field Method" (EDF), a "Gradient Field Method" (GF) or an "Optical Flow Field Method" (OFF) applied to detection and classification of structures of interests in medical images (See for an overview of optical flow computation S. S. Beauchemin *et al.*, "The computation of optical flow," *Comput. Surv.*, vol. 27, no. 3, pp. 433–467, 1995). The present method is based on representing changes in 2-D cross-sections of three-dimensional (3-D) image data (e.g. axial, coronal and sagittal gray scale CTC data) with a vector field, characterizing the topology of this vector field and using the characterized topology of the vector field for detection, identification or recognition tasks of a structure of interest. The present invention could be utilized as a post-processing method that would refine the results of a high sensitivity, low specificity pre-detection by increasing specificity without sacrificing sensitivity. The present invention is, however, not limited to its application as a

post-processing method since it could also be used as an independent method without pre-identification.

The medical images of the present invention are digital or computerized images such as, for instance, but not limited to, a CT, an MRI, a digitized X-ray, or any other medical image application that could be converted or rendered to a digital image. The medical images could be 2-D images used to construct a 3-D image or a 3-D volumetric image. A structure of interest is, for instance, but not limited to, a structure that contains pre-cancerous tissue or cancerous tissue. Examples of structures of interest to a radiologist are, for instance, polyps (such as colonic polyps), nodules (such as liver and lung nodules), lesions, or the like. However, even though the present invention is described with respect to medical images, a person of average skill in the art will readily appreciate that the present invention could easily be applied in any type of application where it is necessary to characterize a structure and determine whether this structure corresponds to a structure of interest.

The first step of the method is the EDF computation to represent the changes in the location of edges in the images (e.g. tissue/air boundaries) as one scrolls through the 3-D data. For instance, as shown in **FIG. 1**, let *xy* be an image plane perpendicular to the scrolling axis *Z* and determine the EDF. In general, one could define at least one image plane or a multiple set of image planes with each scrolling axis perpendicular to its respective/corresponding plane. In one exemplary embodiment, the image planes could be at least two mutually orthogonal planes. A more specific example could be the three anatomical planes and the

scrolling axis defined as the axis perpendicular to its respective plane, i.e. axial, sagittal, coronal. This specific exemplary embodiment of three mutually orthogonal image planes is further described *infra*.

The EDF equation for the *xy* plane is:

$$\nabla I_{z=k} \cdot v_{z=k} + \frac{\partial I_{z=k}}{\partial z} = 0 \qquad (1)$$

where $v_{z=k}(x,y)$ is the EDF defined on the plane that is perpendicular to the z axis and is located at that $z = k$. $I_{z=k}(x,y)$ is the associated image, i.e. the attenuation coefficient function on the same plane. $v_{z=k}(x,y)$ represents the dislocation of the edge at (x, y) along the local gradient from $z = k$ to $z = k+1$. $v_{z=k}(x,y)$ is computed for all k, i.e. for all slices, within the subvolume except at the boundaries. In one example, k could be 25, but k is not limited to 25 and could also be a higher or a lower number. In general, the number for k depends on the maximum polyp size of interest and the data resolution. The positive z direction was defined to be outwards from the center slice. This consistency is required as $v_{z=k}(x,y)$ for all k are summed and (optionally) smoothed to get a composite EDF, $\bar{v}_z(x,y)$, associated with the current subvolume and the scrolling axis Z (see **FIG. 1**; $\bar{v}_z(x,y)$ can be considered as a 2-D representation of a 3-D subvolume of the *xy* plane scrolled over the Z axis). Thus it is assured that the edges of polyp-like structures move inwards on the plane perpendicular to the scrolling axis. The composite EDF could also be

(optionally) smoothed. An example of a smoothing kernel is a Gaussian (σ = 2 mm) whose size could be limited to 2σ. The steps could be completed for all three orthogonal axes (Z = [Axial, Sagittal, Coronal]) resulting in three EDFs that encode information regarding the structure of interest.

The next step is to characterize the vector fields for a single image plane or a combination of image planes. The characterization is based on determining some landmarks in the EDFs. For example, to characterize a single EDF, selected from $\bar{v}_{axial}(x,y)$, $\bar{v}_{coronal}(x,y)$, or $\bar{v}_{sagittal}(x,y)$, one parent node (PN) and a plurality, e.g. eight child nodes (CNs) could be determined. A PN is defined to be the minimum divergence pixel location on the EDF (the PN is marked with a square in **FIGS. 1-3**). In case a pre-detection method is used to detect a structure of interest the PN could be defined to be the minimum divergence pixel location in, for instance, a 4 x 4 mm neighborhood of the pre-detected point on the EDF. CNs are defined to be the pixel locations that are a distance (e.g. 4 mm) away from the PN on the streamlines incoming to the eight immediate neighbors of the PN (CNs are marked with a circle in **FIGS. 1-3**). **FIG. 2** shows an example with three associated axial images and the associated EDF $\bar{v}_{axial}(x,y)$. The parent node (PN) is marked with a square and the children nodes (CNs) are marked with small circles. It is noted that two of the eight CNs coincide with two other CNs.

Each of the EDFs $\bar{v}_{axial}(x,y)$, $\bar{v}_{coronal}(x,y)$ and $\bar{v}_{sagittal}(x,y)$ could be used to compute parameters to classify the structure of interest. As indicated *supra* the classification could

be done using parameters computed from one image plane or a using the parameters computed from a combination of image planes. In one example two parameters, α and β, are computed using the Jacobian matrix of the EDF at the PN (See e.g. J. Helman et al., "Representation and display of vector field topology in fluid flow data sets," *IEEE Computer*, vol. 22, pp. 27–36, Aug. 1989; or Y. Lavin et al., "Feature comparisons of vector fields using earth mover's distance," in *Proc. Visualization'98*, pp. 103–109, 524). The computation of those parameters is as follows:

$$\mathrm{J} = \begin{bmatrix} \frac{\partial \mathbf{v}_x}{\partial x} & \frac{\partial \mathbf{v}_x}{\partial y} \\ \frac{\partial \mathbf{v}_y}{\partial x} & \frac{\partial \mathbf{v}_y}{\partial y} \end{bmatrix} \qquad (2)$$

$$\alpha = \frac{\partial \mathbf{v}_x}{\partial x} + \frac{\partial \mathbf{v}_y}{\partial y} \qquad (3)$$

$$\beta = \frac{\alpha^2 - 4|\mathrm{J}|}{|\alpha^2 - 4|\mathrm{J}||} \sqrt{|\alpha^2 - 4|\mathrm{J}|} \qquad (4)$$

Note that α and β carry information about the eigenvalues of the Jacobian matrix **J**. In fact, the characteristic equation of **J** is:

$$\lambda^2 - \alpha\lambda + |\mathrm{J}| = 0 \qquad (5)$$

Furthermore, α is equal to the divergence of the EDF at PN. β is also computed at the PN and describes the circulatory behavior of EDF at the PN. The ratio of α to β uniquely defines the topology of a linear vector field at the PN so the normalized α and β (normalized by $\sqrt{\alpha^2 + \beta^2}$) are used as suggested by Lavin *et al.* (Y. Lavin et al., "Feature comparisons of vector fields using earth mover's distance," in *Proc. Visualization'98*, pp. 103–109, 524).

Additionally, one could characterize the behavior of the incoming streamlines around the PN using the parameter *d*, defined as:

$$d = \frac{1}{8}\sum_i \left(\sqrt{\sum_j \theta_{ij}^2} \right) \quad \theta_{ij} \le (CN_i, CN_j) \in [0, \pi] \qquad (6)$$

where θ_{ij}'s are computed with respect to the PN's. *d* describes the spread of CNs around the PN. Thus, *d* is used to characterize the spread of CNs around the PN.

FIG. 3 shows an example of four axial EDFs computed for two positive (polyp) and two negative (nonpolyp) cases to provide an understanding of the meaning of EDF characterization parameters visually. In agreement with the intuition, the EDFs

corresponding to positive cases have a PN with an α close to 1 (negative divergence) and β close to zero (small circulatory behavior), and a large d (streamlines well spread around the PN), i.e., a star-shaped topology, unlike the EDFs of negative cases.

Referring back to the exemplary embodiment related to three mutually orthogonal image planes, each parameter could be determined for the axial, coronal, and sagittal EDFs, resulting in a nine-dimensional feature vector for each subvolume considered. In one aspect, one could select to use the mean values of each parameter over three scrolling axes as the final feature vector $f = [\bar{\alpha}, \bar{\beta}, \bar{d}]$ where $\bar{}$ stands for averaging over axial, coronal and sagittal parameters. However, in another aspect one could use other functions and/or criteria of the EDF parameters instead of taking the mean of EDF parameters.

The parameters or the feature vector could now be used to classify the structure of interest. In one example, a binary classification could be established to classify between a polyp versus a non-polyp using a Mahalanobis distance based linear classifier [See PC Mahalanobis, On the generalized distance in statistics, *Proc. Natl. Institute of Science of India* 12:49-55, 1936). The Mahalanobis distance of a vector **f** to the mean vector $\mathbf{m}_\Gamma$ of a population Γ is defined as:

$$r_{f,m_\Gamma} = \sqrt{(f - m_\Gamma)^T C_\Gamma^{-1} (f - m_\Gamma)} \qquad (7)$$

where C_Γ is the covariance matrix of Γ. This distance is a standardized measure that: 1) automatically accounts for scaling; 2) takes care of correlations between features; and 3) can provide linear and curved decision surfaces. For classification purposes, Γ represents the training set and **f** represents a sample from the test set Ω. Referring to the subset of polyps in Γ as Γ_1, and the subset of nonpolyps as Γ_0, the binary classifier is defined as follows:

$$r_{f,m_{\Gamma_1}} - r_{f,m_{\Gamma_0}} + b \leq 0 \Rightarrow f \in \Omega_1$$

$$\text{otherwise} \quad f \in \Omega_0 \tag{8}$$

where Ω_1 and Ω_0 refer to the subsets of polyps and nonpolyps in Ω. An alternative to the Mahalanobis distance-based classifier is the use of SVMs, which minimize training classification error as well as generalization error. In general, the present invention is however, not limited to the selection of a particular classifier.

The present invention has now been described in accordance with several exemplary embodiments, which are intended to be illustrative in all aspects, rather than restrictive. Thus, the present invention is capable of many variations in detailed implementation, which may be derived from the description contained herein by a person of ordinary skill in the art. For instance the present invention has been described in the context of a method, those skilled in the art will appreciate that the method of the present invention is capable of being distributed in the form of a computer readable medium of instructions in a variety of forms,

and that the present invention applies equally regardless of the particular type of signal bearing medium used to actually carry out the distribution. In other words, the present invention is also a program storage device accessible by a computer, tangible embodying a program of instructions or means executable by the computer to perform method steps for detection and classification of a shape in a medical image as described *supra*. Examples of computer readable media include recordable type media such as disks and CD-ROMS and transmission type media such as digital and analog communication links. In addition, the present invention could be implemented and coded in different programming languages and/or packages. All such variations are considered to be within the scope and spirit of the present invention as defined by the following claims and their legal equivalents.